SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET Day	Month	Year
PRIVACY	COSTA RICA		PRIVACY		72 Years	Female	Unk		Unk	

7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data)

Other Serious Criteria: Medically Significant

Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)	Product	Serious	Listed	Reporter Causality	Company Causality
KNEE WEAR [Arthropathy]	XIGDUO XR	Yes	No	Not Applicable	Related
KNEE WEAR [Arthropathy]	FORXIGA	Yes	No	Not Applicable	Related
KIDNEYS WERE DRY [Renal disorder]	XIGDUO XR	No	No	Related	Not Related

(Continued on Additional Information Page)

8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALISATION
- ☒ INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☐ CONGENITAL ANOMALY
- ☒ OTHER

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (include generic name)

#1) XIGDUO XR (DAPAGLIFLOZIN, METFORMIN) Tablet {Lot # TK0174; Exp.Dt. APR-2026}

#2) FORXIGA (DAPAGLIFLOZIN) Film-coated tablet {Lot # tc0024; Exp.Dt. **(Continued on Additional Information Page)**

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ NA

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINISTRATION
#1) 5 milligram, bid	#1) Oral use
#2) 10 milligram, qd	#2) Oral use

17. INDICATION(S) FOR USE

#1) DIABETES (Diabetes mellitus)

#2) DIABETES (Diabetes mellitus) **(Continued on Additional Information Page)**

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ NA

18. THERAPY DATES(from/to)	19. THERAPY DURATION
#1) Unknown / SEP-2023	#1) Unknown
#2) SEP-2023 / Unknown	#2) Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)

23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

From/To Dates	Type of History / Notes	Description
Unknown to Ongoing	Indication	Diabetes (Diabetes mellitus)
Unknown to Ongoing	Indication	Kidney disorder (Renal disorder)

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER

AstraZeneca
Serban Ghiorghiu
1 Medimmune Way
Gaithersburg, Maryland 20878 UNITED STATES
Phone: +1 301-398-0000

26. REMARKS

World Wide #: CR-AstraZeneca-2024A016595
Study ID: PSP-23269
Case References: CR-AstraZeneca-2024A016595

24b. MFR CONTROL NO.

2024A016595

24c. DATE RECEIVED BY MANUFACTURER

02-MAY-2025

24d. REPORT SOURCE

☒ STUDY ☐ LITERATURE ☐ HEALTH PROFESSIONAL ☐ OTHER:

DATE OF THIS REPORT

06-MAY-2025

25a. REPORT TYPE

☐ INITIAL ☒ FOLLOWUP: 3

25b. NAME AND ADDRESS OF REPORTER

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

NAME AND ADDRESS WITHHELD.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)	Product	Serious	Listed	Reporter Causality	Company Causality
KIDNEYS WERE DRY [Renal disorder]	FORXIGA	No	No	Not Applicable	Not Related
VERY TIRED [Fatigue]	XIGDUO XR	No	No	Not Applicable	Not Related
VERY TIRED [Fatigue]	FORXIGA	No	No	Not Applicable	Not Related
ALLERGIC TO METFORMIN [Drug hypersensitivity]	XIGDUO XR	No	No	Not Applicable	Not Related
ALLERGIC TO METFORMIN [Drug hypersensitivity]	FORXIGA	No	No	Not Applicable	Not Related
XIGDUO WASN'T WORKING (LACK OF EFFICACY) [Drug ineffective]	XIGDUO XR	No	No	Related	Not Related
XIGDUO WASN'T WORKING (LACK OF EFFICACY) [Drug ineffective]	FORXIGA	No	No	Not Applicable	Not Applicable
XIGDUO 5MG/1000 TWICE DOSES DAILY (OFF-LABEL USE) [Off label use]	XIGDUO XR	No	No	Not Applicable	Not Related
XIGDUO 5MG/1000 TWICE DOSES DAILY (OFF-LABEL USE) [Off label use]	FORXIGA	No	No	Not Applicable	Not Applicable

Case Description: A solicited report has been received from a consumer in Patient Support Program concerning a female elderly patient born in 1951 (age 72 years).

No medical history was reported. No concomitant products were reported.

During Sep-2023, the patient started treatment with Forxiga (dapagliflozin) (batch number tc0024) (expiration date Jan-2026) 10 milligram qd, Oral use, for diabetes and kidney problems and on an unknown date, with Xigduo Xr (dapagliflozin, metformin) (batch number TK0174) (expiration date Apr-2026) 5 milligram bid, Oral use, for diabetes and kidney problems.

On an unknown date, the patient experienced knee wear (preferred term: Arthropathy), allergic to metformin (preferred term: Drug hypersensitivity), very tired (preferred term: Fatigue) and kidneys were dry (preferred term: Renal disorder).

The report described off-label use for Forxiga, Xigduo Xr. The reported term was xigduo 5mg/1000 twice doses daily (off-label use) (preferred term: Off label use). The report described lack of effect for Xigduo Xr, Forxiga. The reported term was xigduo wasn't working (lack of efficacy) (preferred term: Drug ineffective).

It was unknown if any action was taken with Xigduo Xr. On an unknown date, treatment with Forxiga was discotinued.

On an unspecified date, the patient recovered from the event xigduo wasn't working (lack of efficacy). The outcome of the events of allergic to metformin, kidneys were dry, knee wear, very tired and xigduo 5mg/1000 twice doses daily (off-label use) was unknown.

The reporter assessed the event of knee wear as serious due to disability and medically significant criterion.

The reporter assessed the events of allergic to metformin, kidneys were dry, very tired, xigduo 5mg/1000 twice doses daily (off-label use) and xigduo wasn't working (lack of efficacy) as non-serious.

The reporter did not assess causality for allergic to metformin, kidneys were dry, knee wear, very tired, xigduo 5mg/1000 twice doses daily (off-label use) and xigduo wasn't working (lack of efficacy).The reporter considered that there was a reasonable possibility of a causal relationship between Xigduo Xr and the following event(s): kidneys were dry and xigduo wasn't working (lack of efficacy).
The company physician did not consider that there was a reasonable possibility of a causal relationship between Forxiga and the following event: allergic to metformin, kidneys were dry and very tired.
The company physician did not consider that there was a reasonable possibility of a causal relationship between Xigduo Xr and the following event: allergic to metformin, kidneys were dry, very tired, xigduo 5mg/1000 twice doses daily (off-label use) and xigduo wasn't working (lack of efficacy).
The company physician considered that there was a reasonable possibility of a causal relationship between Forxiga and the following event: knee wear.
The company physician considered that there was a reasonable possibility of a causal relationship between Xigduo Xr and the following event: knee wear.

Summary of follow-up information received by AstraZeneca/MedImmune on 10-Jun-2024 from consumer via solicited source: New events knee wear and allergic to metformin added.Indication added. Narrative updated.Corrected report on 18-Jun-2024: Company causality between the suspect xigduo xr and the events very tired, kidneys were dry and xigduo wasn't working (lack of efficacy) updated to unrelated from related. Company causality for the events kidneys were dry, very tired with suspect forxiga updated to unrelated from related. Narrative amended.

Follow-up of insignificant information received by AstraZeneca/MedImmune on 19-Jun-2024 from consumer via solicited source: New indication added. Narrative updated.

Summary of follow-up information received by AstraZeneca on 02-May-2025 from consumer via Patient Support Program source: Outcome of Drug ineffective was updated from unknown to recovered. Action taken for Xigduo was updated from withdrawn to unknown. Action taken of Farxiga was updated from no change to withdrawn. New dosing regimen added for Xigduo xr. Narrative updated.

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

Company Clinical Comment: Arthropathy is not listed in the core data sheet of Dapagliflozin, Metformin & Dapagliflozin. Due to limited information on underlying comorbidities, past medical history and concomitant medications, complete etiologic and diagnostic workup the evaluation did not find evidence to exclude a reasonable possibility of a causal relationship between Event and suspect drug.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S); 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to); 19. THERAPY DURATION
#1) XIGDUO XR (DAPAGLIFLOZIN, METFORMIN) Tablet {Lot # TK0174; Exp.Dt. APR-2026}; Regimen #1	5 milligram, bid; Oral use	DIABETES (Diabetes mellitus) KIDNEY PROBLEMS (Renal disorder)	Unknown / SEP-2023; Unknown
#1) XIGDUO XR (DAPAGLIFLOZIN, METFORMIN) Tablet; Regimen #2	5 milligram, bid; Oral use	DIABETES (Diabetes mellitus) KIDNEY PROBLEMS (Renal disorder)	Unknown; Unknown
#2) FORXIGA (DAPAGLIFLOZIN) Film-coated tablet {Lot # tc0024; Exp.Dt. JAN-2026}; Regimen #1	10 milligram, qd; Oral use	DIABETES (Diabetes mellitus) KIDNEY PROBLEMS (Renal disorder)	SEP-2023 / Unknown; Unknown